

## WEST Search History





DATE: Wednesday, September 14, 2005

Hide?	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
		<i>DB=PGPB,USPT,EPAB; PLUR=YES; OP=ADJ</i>	
<input type="checkbox"/>	L43	L41 and supra\$	1
<input type="checkbox"/>	L42	L41 and addit\$	1
<input type="checkbox"/>	L41	6190660.pn.	1
<input type="checkbox"/>	L40	L39 and synerg\$	12
<input type="checkbox"/>	L39	L38 and L37	17
<input type="checkbox"/>	L38	(424/130.1  424/134.1  424/135.1  424/138.1  424/141.1  424/142.1  424/155.1  424/156.1)![CCLS]	3244
<input type="checkbox"/>	L37	L36 or L35 or L34	102
<input type="checkbox"/>	L36	L33.clm.	93
<input type="checkbox"/>	L35	L33.ti.	14
<input type="checkbox"/>	L34	L33.ab.	29
<input type="checkbox"/>	L33	L32 or L1	552
<input type="checkbox"/>	L32	CD105	156
<input type="checkbox"/>	L31	L30 and cisplatin	3
<input type="checkbox"/>	L30	L28 not @ay>2001	16
<input type="checkbox"/>	L29	L28 not @py>2001	8
<input type="checkbox"/>	L28	L7 and synerg\$	30
<input type="checkbox"/>	L27	L25 not @ay>2001	13
<input type="checkbox"/>	L26	L14 and chemotherap\$	5
<input type="checkbox"/>	L25	L13 and L1	20
<input type="checkbox"/>	L24	L23 not @ay>2001	7
<input type="checkbox"/>	L23	L22 and synerg\$	28
<input type="checkbox"/>	L22	L21 and L1	76
<input type="checkbox"/>	L21	L20 and L19	163
<input type="checkbox"/>	L20	cancer\$ or tumor\$ or neoplas\$	171759
<input type="checkbox"/>	L19	CD105 or SN6\$	662
<input type="checkbox"/>	L18	L14 and additive	1
<input type="checkbox"/>	L17	L14 and addit\$	7
<input type="checkbox"/>	L16	L14 and synerg\$	0
<input type="checkbox"/>	L15	L14 and L13	0

<input type="checkbox"/>	L14	L1 and SN6\$	7
<input type="checkbox"/>	L13	L12 and synerg\$	20
<input type="checkbox"/>	L12	L11 and doxorubicin	28
<input type="checkbox"/>	L11	L10 and L7	49
<input type="checkbox"/>	L10	L9 or L8	59741
<input type="checkbox"/>	L9	L2.ab.	37849
<input type="checkbox"/>	L8	L2.clm.	39977
<input type="checkbox"/>	L7	L5 or L4 or L3	87
<input type="checkbox"/>	L6	L5 and L4 and L3	11
<input type="checkbox"/>	L5	L1.ti.	14
<input type="checkbox"/>	L4	L1.ab.	26
<input type="checkbox"/>	L3	L1.clm.	80
<input type="checkbox"/>	L2	antibod\$	151295
<input type="checkbox"/>	L1	endoglin	471

END OF SEARCH HISTORY

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1642BJF

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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STN AnaVist, now available  
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NEWS 5 AUG 11 STN AnaVist workshops to be held in North America  
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NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT  
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NEWS HOURS STN Operating Hours Plus Help Desk Availability  
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FILE 'HOME' ENTERED AT 09:06:55 ON 14 SEP 2005

=> file medline

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'MEDLINE' ENTERED AT 09:07:08 ON 14 SEP 2005

FILE LAST UPDATED: 13 SEP 2005 (20050913/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP  
RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s snj?

L1 83 SNJ?

=> s sn6?

L2 42 SN6?

=> s cd105 or antiendoglin or (anti-endoglin) or (anti? (S) endoglin)

244 CD105

0 ANTIENDOGLIN

576495 ANTI

6 ANTIS

576499 ANTI

(ANTI OR ANTIS)

350 ENDOGLIN

17 ANTI-ENDOGLIN

(ANTI (W) ENDOGLIN)

2319481 ANTI?

350 ENDOGLIN

81 ANTI? (S) ENDOGLIN

L3 296 CD105 OR ANTIENDOGLIN OR (ANTI-ENDOGLIN) OR (ANTI? (S) ENDOGLIN)

=> s chemotherap? or anticancer?

180310 CHEMOTHERAP?

17992 ANTICANCER?

L4 193588 CHEMOTHERAP? OR ANTICANCER?

=> s synerg?

L5 83477 SYNERG?

=> s l5 and l3

L6 5 L5 AND L3

=> s l6 and l4

L7 3 L6 AND L4

=> d ibib 1-3

L7 ANSWER 1 OF 3

MEDLINE on STN

ACCESSION NUMBER: 2004470352 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15382054

TITLE: Combination of low-dose cisplatin and recombinant xenogeneic **endoglin** as a vaccine induces **synergistic antitumor** activities.

AUTHOR: Tan Guang-Hong; Tian Ling; Wei Yu-Quan; Zhao Xia; Li Jiong; Wu Yang; Wen Yan-Jun; Yi Tao; Ding Zhen-Yu; Kan Bin; Mao Yong-Qiu; Deng Hong-Xin; Li Hong-Li; Zou Chun-Hua; Fu Chun-Hua

CORPORATE SOURCE: Key Laboratory of Biotherapy of Human Diseases of the Ministry of Education and Cancer Center, West China Hospital, West China Medical School, Sichuan University, Chengdu, People's Republic of China.

SOURCE: International journal of cancer. Journal international du cancer, (2004 Nov 20) 112 (4) 701-6.  
Journal code: 0042124. ISSN: 0020-7136.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200411

ENTRY DATE: Entered STN: 20040922  
Last Updated on STN: 20041117  
Entered Medline: 20041116

L7 ANSWER 2 OF 3 MEDLINE on STN

ACCESSION NUMBER: 2002115119 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11848470

TITLE: Antiangiogenic and antitumor effects of a protein kinase Cbeta inhibitor in human HT-29 colon carcinoma and human CaKil renal cell carcinoma xenografts.

AUTHOR: Teicher B A; Menon K; Alvarez E; Galbreath E; Shih C; Faul M M

CORPORATE SOURCE: Lilly Research Laboratories, Indianapolis, IN 46285, USA..  
TEICHER BEVERLY A@Lilly.com

SOURCE: Anticancer research, (2001 Sep-Oct) 21 (5) 3175-84.  
Journal code: 8102988. ISSN: 0250-7005.

PUB. COUNTRY: Greece

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200203

ENTRY DATE: Entered STN: 20020219  
Last Updated on STN: 20020313  
Entered Medline: 20020312

L7 ANSWER 3 OF 3 MEDLINE on STN

ACCESSION NUMBER: 2001640533 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11691802

TITLE: **Antiangiogenic** therapy of established tumors in human skin/severe combined immunodeficiency mouse chimeras by **anti-endoglin (CD105)** monoclonal **antibodies**, and **synergy** between **anti-endoglin antibody** and cyclophosphamide.

AUTHOR: Takahashi N; Haba A; Matsuno F; Seon B K

CORPORATE SOURCE: Department of Immunology, Roswell Park Cancer Institute, Buffalo, New York 14263, USA.

CONTRACT NUMBER: P30 CA16056 (NCI)

SOURCE: Cancer research, (2001 Nov 1) 61 (21) 7846-54.  
Journal code: 2984705R. ISSN: 0008-5472.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200112

ENTRY DATE: Entered STN: 20011107  
Last Updated on STN: 20020123  
Entered Medline: 20011204

=> d his

(FILE 'HOME' ENTERED AT 09:06:55 ON 14 SEP 2005)

FILE 'MEDLINE' ENTERED AT 09:07:08 ON 14 SEP 2005

L1 83 S SNJ?  
 L2 42 S SN6?  
 L3 296 S CD105 OR ANTIENDOGLIN OR (ANTI-ENDOGLIN) OR (ANTI? (S) ENDOGL  
 L4 193588 S CHEMOTHERAP? OR ANTICANCER?  
 L5 83477 S SYNERG?  
 L6 5 S L5 AND L3  
 L7 3 S L6 AND L4

=> d 16 ibib 1-5

L6 ANSWER 1 OF 5 MEDLINE on STN  
 ACCESSION NUMBER: 2004470352 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 15382054  
 TITLE: Combination of low-dose cisplatin and recombinant xenogeneic **endoglin** as a vaccine induces **synergistic antitumor** activities.  
 AUTHOR: Tan Guang-Hong; Tian Ling; Wei Yu-Quan; Zhao Xia; Li Jiong; Wu Yang; Wen Yan-Jun; Yi Tao; Ding Zhen-Yu; Kan Bin; Mao Yong-Qiu; Deng Hong-Xin; Li Hong-Li; Zou Chun-Hua; Fu Chun-Hua  
 CORPORATE SOURCE: Key Laboratory of Biotherapy of Human Diseases of the Ministry of Education and Cancer Center, West China Hospital, West China Medical School, Sichuan University, Chengdu, People's Republic of China.  
 SOURCE: International journal of cancer. Journal international du cancer, (2004 Nov 20) 112 (4) 701-6.  
 Journal code: 0042124. ISSN: 0020-7136.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200411  
 ENTRY DATE: Entered STN: 20040922  
 Last Updated on STN: 20041117  
 Entered Medline: 20041116

L6 ANSWER 2 OF 5 MEDLINE on STN  
 ACCESSION NUMBER: 2003557567 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 14639611  
 TITLE: **Synergy** between **anti-endoglin** (**CD105**) monoclonal **antibodies** and TGF-beta in suppression of growth of human endothelial cells.  
 AUTHOR: She Xinwei; Matsuno Fumihiko; Harada Naoko; Tsai Hilda; Seon Ben K  
 CORPORATE SOURCE: Department of Immunology, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA.  
 SOURCE: International journal of cancer. Journal international du cancer, (2004 Jan 10) 108 (2) 251-7.  
 Journal code: 0042124. ISSN: 0020-7136.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200401  
 ENTRY DATE: Entered STN: 20031126  
 Last Updated on STN: 20040109  
 Entered Medline: 20040108

L6 ANSWER 3 OF 5 MEDLINE on STN  
 ACCESSION NUMBER: 2003252068 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 12746487  
 TITLE: **CD105** prevents apoptosis in hypoxic endothelial

cells.  
AUTHOR: Li Chenggang; Issa Razao; Kumar Pat; Hampson Ian N;  
CORPORATE SOURCE: Lopez-Novoa Jose M; Bernabeu Carmelo; Kumar Shant  
SOURCE: Department of Pathology, Medical School, University of  
Manchester and Christie Hospital, Manchester M13 9PT, UK.  
Journal of cell science, (2003 Jul 1) 116 (Pt 13) 2677-85.  
Electronic Publication: 2003-05-13.  
Journal code: 0052457. ISSN: 0021-9533.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200404  
ENTRY DATE: Entered STN: 20030531  
Last Updated on STN: 20040420  
Entered Medline: 20040419

L6 ANSWER 4 OF 5 MEDLINE on STN  
ACCESSION NUMBER: 2002115119 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11848470  
TITLE: Antiangiogenic and antitumor effects of a protein kinase  
Cbeta inhibitor in human HT-29 colon carcinoma and human  
CaKil renal cell carcinoma xenografts.  
AUTHOR: Teicher B A; Menon K; Alvarez E; Galbreath E; Shih C; Faul  
M M  
CORPORATE SOURCE: Lilly Research Laboratories, Indianapolis, IN 46285, USA..  
TEICHER BEVERLY A@Lilly.com  
SOURCE: Anticancer research, (2001 Sep-Oct) 21 (5) 3175-84.  
Journal code: 8102988. ISSN: 0250-7005.  
PUB. COUNTRY: Greece  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200203  
ENTRY DATE: Entered STN: 20020219  
Last Updated on STN: 20020313  
Entered Medline: 20020312

L6 ANSWER 5 OF 5 MEDLINE on STN  
ACCESSION NUMBER: 2001640533 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11691802  
TITLE: **Antiangiogenic** therapy of established tumors in  
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by **anti-endoglin (CD105)**  
**monoclonal antibodies**, and **synergy**  
**between anti-endoglin antibody**  
and cyclophosphamide.  
AUTHOR: Takahashi N; Haba A; Matsuno F; Seon B K  
CORPORATE SOURCE: Department of Immunology, Roswell Park Cancer Institute,  
Buffalo, New York 14263, USA.  
CONTRACT NUMBER: P30 CA16056 (NCI)  
SOURCE: Cancer research, (2001 Nov 1) 61 (21) 7846-54.  
Journal code: 2984705R. ISSN: 0008-5472.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200112  
ENTRY DATE: Entered STN: 20011107  
Last Updated on STN: 20020123  
Entered Medline: 20011204

```
=> s chemotherap? or anticancer?
      67803 CHEMOTHERAP?
      32547 ANTICANCER?
L12    95181 CHEMOTHERAP? OR ANTICANCER?
```



=> s l11 and l12  
L13 3 L11 AND L12

=> s l11 not py>2001  
4022896 PY>2001  
L14 3 L11 NOT PY>2001

=> d ibib 1-3

L14 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2002:195484 CAPLUS  
DOCUMENT NUMBER: 137:210512  
TITLE: Antiangiogenic and antitumor effects of a protein  
kinase CB inhibitor in human HT-29 colon  
carcinoma and human CaKil renal cell carcinoma  
xenografts  
AUTHOR(S): Teicher, Beverly A.; Menon, Krishna; Alvarez, Enrique;  
Galbreath, Elizabeth; Shih, Chuan; Faul, Margaret M.  
CORPORATE SOURCE: Lilly Research Laboratories, Lilly Corporate Center,  
Indianapolis, IN, 46285, USA  
SOURCE: Anticancer Research (2001), 21(5), 3175-3184  
CODEN: ANTRD4; ISSN: 0250-7005  
PUBLISHER: International Institute of Anticancer Research  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2001:832793 CAPLUS  
DOCUMENT NUMBER: 136:95741  
TITLE: **Antiangiogenic** therapy of established tumors  
in human skin/severe combined immunodeficiency mouse  
chimeras by **anti-endoglin** (  
**CD105**) monoclonal **antibodies**, and  
**synergy** between **anti-**  
**endoglin antibody** and  
cyclophosphamide  
AUTHOR(S): Takahashi, Norihiko; Haba, Akinao; Matsuno, Fumihiko;  
Seon, Ben K.  
CORPORATE SOURCE: Department of Immunology, Roswell Park Cancer  
Institute, Buffalo, NY, 14263, USA  
SOURCE: Cancer Research (2001), 61(21), 7846-7854  
CODEN: CNREA8; ISSN: 0008-5472  
PUBLISHER: American Association for Cancer Research  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1996:32553 CAPLUS  
DOCUMENT NUMBER: 124:114613  
TITLE: Hodgkin's disease and anaplastic large cell lymphoma  
revisited. 1. Unique cytokine and cytokine receptor  
profile distinguished from that of non-Hodgkin's  
lymphomas  
AUTHOR(S): Hsu, Su-Ming; Waldron, James; Xie, Su-Su; Hsu,  
Pei-Ling  
CORPORATE SOURCE: John L. McClellan Veterans Hospital, Little Rock, AR,  
72205, USA  
SOURCE: Journal of Biomedical Science (Basel) (1995), 2(4),

302-13  
CODEN: JBCIEA; ISSN: 1021-7770  
Karger  
Journal; General Review  
English

PUBLISHER:  
DOCUMENT TYPE:  
LANGUAGE:

=> d kwic 3

L14 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN  
AB . . . H-RS/ALCL cells may express cytokine receptors (R), such as CD30, CD40, IL-2R (CD25/CD122), IL-6R (CD126), IL-7R (CD127), TNF-R (CD120), TGF- $\beta$ R ( **CD105**/endoglin), M-CSFR (CD115), and SCFR (CD117/c-kit receptor). All of these cytokines and cytokine receptors are implicated in the growth regulation of. . . in conjunction with IL-9 and/or CD117 may be regarded as unique for HD/ALCL because of an unusual combination and a **synergistic** activity among these cytokines. The expression of CD70 and CD80/CD86 (as cytokines) may exert a unique effect in HD because. . .

=> d ibib ab 3

L14 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1996:32553 CAPLUS  
DOCUMENT NUMBER: 124:114613  
TITLE: Hodgkin's disease and anaplastic large cell lymphoma revisited. 1. Unique cytokine and cytokine receptor profile distinguished from that of non-Hodgkin's lymphomas  
AUTHOR(S): Hsu, Su-Ming; Waldron, James; Xie, Su-Su; Hsu, Pei-Ling  
CORPORATE SOURCE: John L. McClellan Veterans Hospital, Little Rock, AR, 72205, USA  
SOURCE: Journal of Biomedical Science (Basel) (1995), 2(4), 302-13  
CODEN: JBCIEA; ISSN: 1021-7770  
PUBLISHER: Karger  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review with 123 refs. In cultures, and in tissues as well, Hodgkin's and Reed-Sternberg (H-RS) cells and anaplastic large cell lymphoma (ALCL) cells are known to express a variety of cytokines, including IL-1, -5, -6, -8, -9, TNF- $\alpha$ , GM-CSF, M-CSF, TGF- $\beta$ , CD70, CD80, and CD86. Various nos. of H-RS/ALCL cells may express cytokine receptors (R), such as CD30, CD40, IL-2R (CD25/CD122), IL-6R (CD126), IL-7R (CD127), TNF-R (CD120), TGF- $\beta$ R ( **CD105**/endoglin), M-CSFR (CD115), and SCFR (CD117/c-kit receptor). All of these cytokines and cytokine receptors are implicated in the growth regulation of H-RS/ALCL cells, the histopathol. alterations in tissues, and the clin. manifestations in patients with Hodgkin's disease (HD) or ALCL. Many of these cytokines or cytokine receptors also play an important role in the pathogenesis of other types of lymphomas. In this review, the authors describe the cytokine or cytokine-receptor expression that is diacritic for H-RS/ALCL cells. The identification of such unique cytokine-cytokine receptor interactions is likely to explain the biol. property that distinguishes HD/ALCL from other types of lymphomas. These interactions include those of CD30L-CD30, CD40L-CD40, CD70-CD27, CD80/CD86-CD28, SCF-CD117, IL-9-IL9R, and IL-7-IL7R. The H-RS/ALCL cells express IL-9 and two cytokine receptors, CD30 and CD117, which are observed infrequently in NHLs. Although IL-7 expression is not restricted to H-RS/ALCL cells, the expression of IL-7 in conjunction with IL-9 and/or CD117 may be regarded as unique for HD/ALCL because of an unusual combination and a **synergistic** activity

among these cytokines. The expression of CD70 and CD80/CD86 (as cytokines) may exert a unique effect in HD because of intimate contact between H-RS cells and CD27/CD28-pos. T cells. The expression of these costimulators (CD70 and CD80/CD86) and other adhesion/costimulator mols. such as CD54 and CD58, along with the secretion of soluble cytokines such as IL-1, IL-6, IL-7, or TNFs by H-RS/ALCL cells, could result in the profound T-cell proliferation often seen in lymph nodes involved by HD and some ALCL. The expression of CD30L and CD40L by surrounding T cells may affect the proliferation of H-RS/ALCL cells. The cytokine-cytokine receptor interaction between H-RS cells and T cells via direct cell-cell contact is bidirectional, a situation not commonly seen in NHLs.

=> file pctfull		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	28.20	31.67
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-1.46	-1.46

FILE 'PCTFULL' ENTERED AT 09:12:09 ON 14 SEP 2005  
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FILE LAST UPDATED: 6 SEP 2005 <20050906/UP>  
MOST RECENT UPDATE WEEK: 200535 <200535/EW>  
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

```
=> s cd105 or antiendoglin or (anti-endoglin) or (anti? (S) endoglin)
    129 CD105
      0 ANTIENDOGLIN
    160674 ANTI
      158 ANTIS
    160703 ANTI
      (ANTI OR ANTIS)
      303 ENDOGLIN
      15 ANTI-ENDOGLIN
      (ANTI (W) ENDOGLIN)
    282747 ANTI?
      303 ENDOGLIN
      199 ANTI? (S) ENDOGLIN
L15    286 CD105 OR ANTIENDOGLIN OR (ANTI-ENDOGLIN) OR (ANTI? (S) ENDOGLIN)
```

```
=> s synerg?
L16    32472 SYNERG?
```

```
=> s l15 and l16
L17    68 L15 AND L16
```

```
=> s chemotherap? or anticancer?
      27871 CHEMOTHERAP?
      13352 ANTICANCER?
L18    34531 CHEMOTHERAP? OR ANTICANCER?
```

```
=> s l17 and l18
L19    51 L17 AND L18
```

```
=> s l15/ab
      5 CD105/AB
      0 ANTIENDOGLIN/AB
```

19384 ANTI/AB  
 1 ANTIS/AB  
 19384 ANTI/AB  
 ((ANTI OR ANTIS)/AB)  
 4 ENDOGLIN/AB  
 1 ANTI-ENDOGLIN/AB  
 ((ANTI(W) ENDOGLIN)/AB)  
 56517 ANTI?/AB  
 4 ENDOGLIN/AB  
 1 ANTI?/AB (S) ENDOGLIN/AB  
 L20 6 (CD105/AB OR ANTIENDOGLIN/AB OR (ANTI-ENDOGLIN/AB) OR (ANTI?/AB  
 (S) ENDOGLIN/AB))

=> s 120 and 116

L21 1 L20 AND L16

=> d ibib 1

L21 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2005 Univentio on STN  
 ACCESSION NUMBER: 2005017117 PCTFULL ED 20050302 EW 200508  
 TITLE (ENGLISH): MULTIPOTENT AMNIOTIC FETAL STEM CELLS (MAFSC) AND  
 BANKING OF SAME  
 TITLE (FRENCH): CELLULES SOUCHES FOETALES AMNIOTIQUES PLURIPOTENTES  
 (MAFSC) ET CONSTITUTION DE BANQUES DE CELLES-CI  
 INVENTOR(S): HAAS, Martin, 4888 Drakewood Terrace, San Diego, CA  
 92130, US [US, US]  
 PATENT ASSIGNEE(S): HAAS, Martin, 4888 Drakewood Terrace, San Diego, CA  
 92130, US [US, US]  
 AGENT: HART, Daniel\$, Knobbe Martens Olson & Bear LLP, 2040  
 Main Street, 14th Floor, Irvine, CA 92614\$, US  
 LANGUAGE OF FILING: English  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2005017117	A2	20050224

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO  
 CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR  
 HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV  
 MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO  
 RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ  
 VC VN YU ZA ZM ZW

RW (ARIPO): BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW  
 RW (EAPO): AM AZ BY KG KZ MD RU TJ TM  
 RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU  
 MC NL PL PT RO SE SI SK TR  
 RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2004-US26304 A 20040813  
 PRIORITY INFO.: US 2003-60/495,513 20030814  
 US 2003-60/495,437 20030814

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L21 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2005 Univentio on STN  
 ABEN . . . cells are characterized by the following cell surface markers:  
 SSEA3, SSEA4, Tra-1-60, Tra-1-81, Tra-2-54, HLA class I, CD13, CD44,  
 CD49b, CD105 and are distinguished by the absence of the  
 antigen markers CD34, CD45, and HLA Class II, but are distinguished  
 from. . .  
 ABFR . . . sont caracterisees par les marquers de surface cellulaire

suivants: SSEA3, SSEA4, Tra-1-60, Tra-1-81, Tra-2-54, HLA classe I, CD13, CD44, CD49b, **CD105** et se distinguent par l'absence de marqueurs d'antigenes CD34, CD45, et HLA Classe II, mais se distinguent des cellules souches. . . de personnes enceintes. Les cellules derivees de fluides amniotiques sont placees dans des banques pour permettre l'acces aux cellules souches **synergiques** pluripotentes ou compatibles avec des antigenes de transplantation.

=> d his

(FILE 'HOME' ENTERED AT 09:06:55 ON 14 SEP 2005)

FILE 'MEDLINE' ENTERED AT 09:07:08 ON 14 SEP 2005

L1 83 S SNJ?  
L2 42 S SN6?  
L3 296 S CD105 OR ANTIENDOGLIN OR (ANTI-ENDOGLIN) OR (ANTI? (S) ENDOGL  
L4 193588 S CHEMOTHERAP? OR ANTICANCER?  
L5 83477 S SYNERG?  
L6 5 S L5 AND L3  
L7 3 S L6 AND L4  
L8 3 S CAPLUS

FILE 'CAPLUS' ENTERED AT 09:09:59 ON 14 SEP 2005

L9 313 S CD105 OR ANTIENDOGLIN OR (ANTI-ENDOGLIN) OR (ANTI? (S) ENDOGL  
L10 100162 S SYNERG?  
L11 8 S L9 AND L10  
L12 95181 S CHEMOTHERAP? OR ANTICANCER?  
L13 3 S L11 AND L12  
L14 3 S L11 NOT PY>2001

FILE 'PCTFULL' ENTERED AT 09:12:09 ON 14 SEP 2005

L15 286 S CD105 OR ANTIENDOGLIN OR (ANTI-ENDOGLIN) OR (ANTI? (S) ENDOGL  
L16 32472 S SYNERG?  
L17 68 S L15 AND L16  
L18 34531 S CHEMOTHERAP? OR ANTICANCER?  
L19 51 S L17 AND L18  
L20 6 S L15/AB  
L21 1 S L20 AND L16

=> s l19 not py>2000

506539 PY>2000

L22 13 L19 NOT PY>2000

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L22 ANSWER 4 OF 13 PCTFULL COPYRIGHT 2005 Univentio on STN  
ACCESSION NUMBER: 2000002584 PCTFULL ED 20020515  
TITLE (ENGLISH): CANCER TREATMENT METHODS USING ANTIBODIES TO  
AMINOPHOSPHOLIPIDS  
TITLE (FRENCH): PROCEDES DE TRAITEMENT DU CANCER REPOSANT SUR  
L'UTILISATION D'ANTICORPS VIS-A-VIS DES  
AMINOPHOSPHOLIPIDES  
INVENTOR(S): THORPE, Philip, E.;  
RAN, Sophia  
PATENT ASSIGNEE(S): BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM  
LANGUAGE OF PUBL.: English  
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DESIGNATED STATES

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK  
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP  
 KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL  
 PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU  
 ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD  
 RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC  
 NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 1999-US15600 A 19990712  
 PRIORITY INFO.: US 1998-60/092,672 19980713  
 US 1998-60/110,608 19981202

DETD . . . is a particular advantage, although the invention provides various effective compositions and combinations thereof

## 2, Description of the Related Art

Tumor cell resistance to **chemotherapeutic** agents represents a significant problem in clinical oncology. In fact, this is one of the main reasons why many of the most prevalent forms of human cancer still resist effective **chemotherapeutic** intervention, despite certain advances in the field of **chemotherapy**.

tumors. e.g., lymphomas, and tumors of the blood and blood-forming organs, e.g., leukemias, have generally been more responsive to **chemotherapeutic** therapy than have solid tumors, such as carcinomas.

One reason for the susceptibility of soft and blood-based tumors to **chemotherapy** is the greater accessibility of lymphoma and leukemic cells to

**chemotherapeutic** intervention. Simply put, it is much more difficult for most

**chemotherapeutic** agents to reach all of the cells of a solid tumor mass than it is the soft tumors and blood-based tumors, and therefore much more difficult to achieve a

total cell kill. Increasing the dose of **chemotherapeutic** agents most often results in toxic side effects, which generally limits the effectiveness of conventional anti-tumor agents.

immunotoxin., in which an anti-tumor cell antibody is used to deliver a toxin to the tumor cells. However, in common with the **chemotherapeutic** approaches described above, immunotoxin therapy also suffers from significant drawbacks. For example, antigen-negative or antigen-deficient cells can survive and repopulate the tumor. . .

The one or more additional anti-cancer agents may be

**chemotherapeutic** agents, radiotherapeutic agents, cytokines, anti-angiogenic agents, apoptosis-inducing agents or anti-cancer immunotoxins or coaguligands.

**Chemotherapeutic** agents, as used herein, refer to classical **chemotherapeutic** agents or drugs used in the treatment of malignancies. This term is used for simplicity notwithstanding the fact

that other compounds may be technically described as **chemotherapeutic** agents in that they exert an anti-cancer effect. However, **chemotherapeutic** has come to have a distinct meaning in the art and is being used according to this standard meaning. A number of exemplary chemotherapeutic agents are described herein. Those of ordinary skill in the art will readily understand the uses and appropriate doses of **chemotherapeutic** agents, although the doses may well be reduced when used in combination with the present invention. A new class of drugs that may also be termed

**chemotherapeutic** agents are agents that induce apoptosis. Any one or more of such drugs, including genes, vectors and antisense constructs, as appropriate, . . .

**Anti-tumor** vasculature immunotoxins or coaguligands may comprise ligands,

**antibodies**, or fragments thereof, that bind to a surface-expressed, surface-accessible or surface-localized component of the blood transporting vessels, preferably the intratumoral blood vessels, of a vascularized tumor. Such **antibodies** include those that bind to surface-expressed components of intratumoral blood vessels of a vascularized tumor, including aminophospholipids themselves, and intratumoral vasculature cell surface receptors, such as **endoglin** (TEC-4 and TEC-1 **antibodies**), a TGF $\beta$  receptor, E-selectin, P-selectin, VCAM-1, ICAM-1, PSMA, a VEGFR receptor, an FGF receptor, a TIE,  $\alpha$ 3 integrin, pleiotropin, endosialin and MHC Class II proteins. The **antibodies** may also bind to cytokine-inducible or coagulant-inducible components of intratumoral blood vessels.

anti-PS, anti-PE, human, humanized and monoclonal antibodies, or fragments thereof, being preferred. The anti-cancer agents are also those as described above, including **chemotherapeutic** agents, radiotherapeutic agents, anti-angiogenic agents, apoptotic agents, immunotoxins and coaguligands. Agents formulated for intravenous administration will often be preferred.

One of the present inventors has been developing **anti-tumor** vasculature immunotoxins and coaguligands for therapeutic use for some time (for example, see U.S. Patent Nos. 5,585,866 and 5,877,289, and U.S. Applications. . . . Serial Nos. 08/350,212, 08/487,427 and 08/482,369; Issue Fees paid; each incorporated herein by reference). In the non-natural course of these studies, various **antibodies**,

including **anti-Class 11**, **anti-endoglin**, **anti-VCAM- I** and **anti-VEGF.**, have been administered to tumor-bearing animals and shown to specifically localize to the intratumoral vasculature. Following such confirmation, the **antibodies** are linked to the toxic or coagulative effector portion to form an immunotoxin or coaguligand, which is then administered to exert an **anti-tumor** effect.

acceptable formulations, either for diagnosis/imagino or combined therapy. For example, such kits may contain any one or more of a range of **chemotherapeutic** or radiotherapeutic drugs; anti-angiogenic agents; anti-tumor cell antibodies; and/or anti-tumor vasculature or anti-tumor stroma immunotoxins or coaguligands.

is most preferably exploited for the treatment of solid tumors. Such uses may employ anti-aminophospholipid antibodies alone or in combination with **chemotherapeutic**, radiotherapeutic, apoptotic, anti-angiogenic agents and/or immunotoxins or coaguligands. The anti-aminophospholipid antibody methods provided by this invention are broadly applicable to the treatment of. . .

antibody therapy of the invention may predispose the tumor to further therapeutic treatment, such that the subsequent treatment results in an overall **synergistic** effect or even leads to total remission or cure.

one course of conventional therapy, and will have objectively measurable disease as determined by physical examination, laboratory techniques, and/or radiographic procedures. Any **chemotherapy** should be stopped at least 2 weeks before entry into the study. Where murine monoclonal antibodies or antibody portions are employed, the. . .

In connection solid tumor treatment, the present invention may be used in combination with classical approaches, such as surgery, radiotherapy, **chemotherapy**, and the like. The invention therefore provides combined therapies in which anti-aminophospholipid antibodies are used simultaneously with, before, or after surgery or radiation treatment; or are administered to patients with, before, or after conventional **chemotherapeutic**, radiotherapeutic or anti-angiogenic agents, or targeted immunotoxins or coaguligands.

one of the single therapies would be of benefit. Also, there is no particular requirement for the combined treatment to exhibit **synergistic** effects,



although this is certainly possible and advantageous. Agents particularly contemplated for use in achieving potentially **synergistic** effects are those that injure, or induce apoptosis in, the tumor endothelium, as such injury or apoptosis should amplify the overall therapeutic. . .

#### **J1. Chemotherapeutics**

In certain embodiments, the anti-aminophospholipid antibodies of the present invention may be administered in combination with a **chemotherapeutic** agent.

**Chemotherapeutic** drugs can kill proliferating tumor cells, enhancing the necrotic areas created by the overall treatment. The drugs can thus enhance the. . .

By inducing the formation of thrombi in tumor vessels, the anti-aminophospholipid antibodies can enhance the action of the **chemotherapeutics** by retaining or trapping the drugs within the tumor. The **chemotherapeutics** are thus retained within the tumor, while the rest of the drug is cleared from the body. Tumor cells are thus exposed. . .

Irrespective of the underlying mechanism(s), a variety of **chemotherapeutic** agents may be used in the combined treatment methods disclosed herein.

**Chemotherapeutic** agents contemplated as exemplary include, e.g., tamoxifen, taxol, vincristine, vinblastine, etoposide (VP-16), adriamycin, 5-fluorouracil (5FU), camptothecin, actinomycin-D, mitomycin C, cisplatin (CDDP), combretastatin(s). . .

As will be understood by those of ordinary skill in the art, the appropriate doses of **chemotherapeutic** agents will be generally around those already employed in clinical therapies wherein the chemotherapeutics are administered alone or in combination with other **chemotherapeutics**. By way of example only, agents such as cisplatin, and other DNA alkylating may be used. Cisplatin has been widely used. . .

Further useful agents include compounds that interfere with DNA replication, mitosis, chromosomal segregation and/or tubulin activity. Such **chemotherapeutic** compounds include adriamycin, also known as doxorubicin, etoposide, verapamil, podophyllotoxin(s), combretastatin(s) and the like. Widely used in a clinical setting for the treatment. . .

Exemplary **chemotherapeutic** agents that are useful in connection with I 0 combined therapy are listed in Table B. Each of the agents listed.

TABLE B

**Chemotherapeutic Agents Useful in Neoplastic Disease**

NONPROPRIETARY

CLASS TYPE OF AGENT NAMES DISEASE

(OTHER NAMES)

Mechlorethamine (HN2 Hodgkin's disease, non-Hodgkin's lymphomas)

Acute and chronic lymphocytic leukemias, Hodgkin's.

or ligand, is directed to a relatively specific marker of the tumor cells, tumor vasculature or tumor stroma. In common with the **chemotherapeutic** and anti-angiogenic agents discussed above, the use of an anti-aminophospholipid antibody in combination with a targeted toxin or coagulant will generally result. . . distinct agents being directed against different targets within the tumor environment. This should result in additive, markedly greater than additive or even **synergistic** anti-tumor results.

or  
'body conjugate, that, when administered in vivo, will produce only negligible or anti clinically manageable side effects, such as those normally encountered during **chemotherapy**.

For tumor vasculature targeting, the targeting **antibody** or ligand will often bind to a marker expressed by, adsorbed to, induced on or otherwise localized to the intratumoral blood vessels of a vascularized tumor. Appropriate expressed target molecules include, for example, **endoglin**, E-selectin, P-selectin, VCAM-1, ICAM-1, PSMA (Liu et al., 1997), a TIE, a ligand reactive with LAM-1, a VEGFNPFR receptor, an FGF receptor, . . . those such as VEGF, FGF, TGFP, HGF, PF4, PDGF, TIMP, a ligand that binds to a TIE and tumor-associated fibronectin isoforms. **Antigens** naturally and artificially inducible by cytokines and coagulants may also be targeted, such as ELAM-1, VCAM-1, ICAM-1, a ligand reactive with LAM-1, **endoglin**, and even MHC Class II (cytokine-inducible, e.g., by IL-1, TNF- $\alpha$ , IFN- $\gamma$ , IL-4 and/or TNF- $\beta$  and E-selectin, P-selectin, PDGF and ICAM-1 (coagulant-inducible e.g., . . .

otherwise anti-cellular agents having the ability to kill or suppress the growth or cell division of endothelial cells. Suitable anti-cellular agents include **chemotherapeutic** agents and radioisotopes, as well as cytotoxins. Exemplary **chemotherapeutic** agents include: steroids; cytokines; anti-

metabolites, such as cytosine arabinoside, fluorouracil, methotrexate or aminopterin; anthracyclines; mitomycin C; vinca alkaloids; antibiotics; demecolcine; etoposide; mithramycin; . . .

A variety of **chemotherapeutic** and other pharmacological agents can also be successfully conjugated to antibodies or targeting ligands. Exemplary antineoplastic agents that have been conjugated to. . .

MECA 32, a pan **anti-mouse** vascular endothelial cell **antibody**, was prepared as described by Leppink et al. (1989, incorporated herein by reference). MJ 7/18 rat IgG, reactive with murine **endoglin**, was prepared as described by Ge and Butcher (1994, incorporated herein by reference). The MECA 32 and MJ 7/18 **antibodies** served as positive controls for immunohistochemical studies.

Overall, VCAM-I expression was observed on 20-30% of total tumor blood vessels stained by the **anti-endoglin antibody**, MJ 7/18. VCAM-I staining of the tumor vessels was largely observed on venules. VCAM-I expression was similar in tumors up to 1500. . .

CLMEN. . . provide exemplary procedural or other details supplementary to those set forth herein, are specifically incorporated herein by reference.

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 36 The kit of any one of claims 32 through 35, wherein said second anti-cancer agent is a **chemotherapeutic**, radiotherapeutic, anti-angiogenic or apoptosis-inducing agent.  
 41 The kit of claim 40, wherein said targeting **antibody**, or **antigen**-binding fragment thereof, binds to a surface-expressed component of intratumoral vasculature selected from the group consisting of an aminophospholipid, **endoglin**, a TGF $\beta$  receptor, E-selectin, P-selectin, VCAM-1, ICAM-1, PSMA, a VEGFNPF



receptor, an  
FGF receptor, a TIE, UA integrin, pleiotropin, endosialin and an. . .

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L22 ANSWER 13 OF 13 PCTFULL COPYRIGHT 2005 Univentio on STN  
ACCESSION NUMBER: 1996021416 PCTFULL ED 20020514  
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DETD Backg[ound of the Inymfim  
Many different therapies are available for treatment of various types of human tumors. These include surgery, radiotherapy, **chemotherapy**, radioimmunotherapy, and neoadjuvant therapy. These treatments can be used indhridually or in combination, depending on whether the tumor is metastasizing or non-metastasizing.  
intent for certain tumors. For more adensive cancers, radiation is combined with surgery. Radiation is also used as an adjuvant to **chemotherapy** for some patients with lymphoma or lung cancer and for several cancers in ]hildren. Occasionally, **chemotherapy** may be used to sensitize tumor cells to the toxic effects of radiation.

**Chemotherapy** is used when surgery or radiation is not practical or only partially effective. **Chemotherapy**, involving the use of cytoldnes, cytotoxic drugs, hormones, antihormones, and other biological agents, has become an increasingly effective means of treating cancer.. . .

While most **anticancer** drugs are used systemically, there are selected indications for local or regional administration. Regional administration involves direct infusion of active **chemotherapeutic** agents into the tumor site (eg., intravesical therapy, intraperitoneal

therapy, hepatic artery infusion with or without embolization of the main blood. . . .

However, many patients treated with **chemotherapy** have a limited response. Such treatment may become ineffective because of drug resistance attributed to spontaneous genetic mutations in subpopulations of cancer cells prior to **chemotherapy** exposure.

Following elimination of the sensitive cells by **chemotherapy**, the resistant subpopulation grows to become the predominant cell type. I Radioimmunotherapy is a form of treatment that offers the potential for.

. . . . show similar efficacy in other animal models and clinical trials (Kao, et al., Behring Inst. Mill. 92:92, 1993), it was reasoned that unique **synergistic** cofactors were produced by Meth-A cells that sensitized the tumors to TNF. Two such factors, endothelial-monocyte-activating polypeptides I and II (E-I, EMAP-II), . . . . 269:9774, 1994). TNF and EMAP-I and H aU induce weak tissue factor activity in 30 endothelial cells and monocytes but act **synergistically** when combined (Kao, et al., supra; Clauss, et al., J. Biol. Chem. 265:7078, 1990). This synergistic effect may be utilized. . . .

. . . . domains of VEGF. Such ligands include, but are not limited to, TGF- $\beta$ , FGF, PDGF, u-PA, u-PA receptor antagonist, and ligands for **endoglin**, endothelial CD31, CD34, integrin  $\alpha$ V $\beta$ 3, and **antigen** binding fragments of monoclonal **antibodies** reactive against receptors found on endothelial cells.

. . . . antifungal agent 5-fluorocytosine (5-FC). Cytosine deaminase converts 5-FC to 5-fluorouracil (5-FU, Nishiyama, et al., Cancer Res. 45:1753, 1985). Since 5-FU is commonly used

. . . . **chemotherapeutic** drug for breast cancer, several groups have developed cytosine deaminase-based 'suicide gene' therapy models for this disease. Tumor specificity may . . . of antibody directed enzyme-prodrug therapy (ADEPT). This enzyme has the advantage that it can activate a wide range of phosphorylated derivatives of **anticancer** agents (e.g.

. . . . cross cell membranes until the charged phosphate group is cleaved off, so a single enzyme could generate de novo a cocktail of

. . . . **chemotherapeutic** agents within the tumor mass (Senter, et al., Bioconjugate Chem. 4:3, 1993). Other suicide genes may encode a polypeptide or polypeptides. . . .

. . . . folate receptor (see below) and are partially or completely growth-inhibited by folate deprivation (Matsue, et al., PNAS

89:6006, 1992). A family of **chemotherapeutic** drugs that includes methotrexate exert their antitumor activity by antagonism of the folate pathway (Koong-Nah, et al., J Clin. Invest.

engineered to contain an avidin domain (that binds specifically to biotin) and then complexed with biotinyl derivatives of any of several monoclonal **antibodies** (MAbs) that are selective or specific for capillary endothelial cells in solid tumors. Several such reagents have been described in the. . . is absent from the vasculature of normal tissues (Rettig, et al, PNAS 89:10832, 1989); TEC-4 and TEC- I 1, which react with **endoglin** (CD105), a Type HI TGF3 receptor that is upregulated; and LM609, a MAb that recognizes a conformational determinant formed by epitopes from. . .